UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/081,076 | 02/20/2002 | Paul A. Barstad | 252312006002 | 4811 |

25226 7590 09/29/2005

MORRISON & FOERSTER LLP
755 PAGE MILL RD
PALO ALTO, CA 94304-1018

| EXAMINER | |
|---|---|
| SAUNDERS, DAVID A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | |

DATE MAILED: 09/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/081,076 | BARSTAD ET AL. | |
| | Examiner | Art Unit | |
| | David A. Saunders, PhD | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *21 March 2005 and 08 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *28,29,31-40,42 and 43* is/are pending in the application.

4a) Of the above claim(s) *33-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28,29,31,32,38-40,42 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Amendments of 3/21/05 and 7/8/05 of have been entered. Claims 28-29,31-40 and 42-43 are pending. Claims 28-29,31-32,38-40 and 42-43 are under examination. The amendment has entered no new matter.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The amendment has overcome previously stated issues as follows:

The objection(s) to the specification.

The rejection of claims 28-32 and 38-43 under 35 USC 112, 2nd paragraph.

The prior art rejections based upon Tanihara et al, over Millich et al, and over Good et al.

The following rejection(s) of record are maintained or modified as follows:

Claims 31 and 42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 31 and 42 are rejected as containing new matter because a generic "buffer" is not supported by the specific recitation of "0.1m sodium borate buffer, PH 9.0" at page 13, Lines 26-27.

Applicant has urged that "one of skill in the art" would have recognized that various buffers were "well known in the art" for the purpose of dissolving peptides. These are arguments that pertain to overcoming a scope of enablement rejection under 112, first para. or an obviousness rejection under 103, rather than a description rejection under 112, first para. The description requirement is separate from the enablement requirement of 112, first para. (Vas Cath v. Mahurkar 19 USPQ2d 1111); and the description requirement cannot be satisfied by urging what might be obvious (Lockwood v. American Airlines 41 USPQ2d 1961).

Claims 32 and 43 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial asserted utility or a well established utility.

While applicant has described complexes of the immunogen analogs and antibodies as being formed in immunoassays, he has not disclosed a use for the complexes per se. These assay are disclosed (page 8, Lines 29+) as being conducted for the purpose of identifying useful immunogen analogs, not for obtaining the complexes. Further the title, abstract, technical Field, Disclosure of the invention, and taught therapeutic utilities (page 12, lines 4+) teach nothing about the use of analogue - antibody complexes, nor of any compositions containing such complexes.

Claims 32 and 43 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant has urged that the antigen-antibody complexes have utility as an indicator in an assay for finding immunogen analogues. The rejection is maintained because the taught assays make further use of the immunogen analogues identified, not of the antigen antibody complexes that are incidentally formed in the assay.

Claim 28 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,060,056. Although the conflicting claims are not identical, they are not patentably distinct from each other because it is considered in the public interest to require a disclaimer to assure common ownership.

Firstly, it is noted that the instant claims, drawn to polypeptide analogues, claim a precursor compound for the synthesis of the conjugates claimed in Pat. No. 6,060,056. It is noted that the instant claims may be considered as drawn to the element A (analogue) while the issued claims may be considered as drawn to A incorporated into ' the combination A + L + P, in which L is a conjugating Linker and P is a platform molecule. Since applicant could have earlier claimed A alone, and since claiming A with "comprising" encompasses claiming the conjugate, the requirement for a disclaimer is considered proper.

It is to be noted that the relationship between the instant and patented claims is like that of In re Borah 148 USPQ 213 and of General Foods Corp. 23 USPQ2d 1839. In both cases the pending claims recited less than the total number of elements recited in the issued claim. In each case the office was found in error to require a disclaimer for the broader claims reciting less than the issued claims. The Office presently considers

the requirement proper because the instant fact situation does not exactly parallel Borah and General Foods. In those causes, the patented claims arose from a second filed application, which was disclosed as an improvement over a first filed application, which disclosed a broader invention for which the claims were still pending. instantly, however, there was no second filed application disclosing an improvement of the invention of an earlier filed application. In Pat.'056 applicant chose to go for the more narrow claims reciting the combination A+L+P. Though he could have claimed A alone, he never even presented such claims.

Applicant has indicated that a disclaimer will be filed upon the indication that claims are otherwise allowable.

Applicant's arguments filed 3/21/05 have been fully considered but they are not persuasive with respect to claims 28, 31-32 and 42-43 for the reasons stated above.

Upon reconsideration the following grounds of rejection are newly stated.

Claims 38-40 and 42-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 38 "a T-cell stimulation index below about 2-3" is indefinite because "2-3" has no units and/or "2-3" is not defined relative to any basis. Likewise note claim 39.

Also, in claim 39, recitation of "in an individual" is unclear because this implies an in vivo test, while what applicant has disclosed is an in vitro T-cell stimulation test.

For prior art considerations, the claims are given benefit of the fling date of ultimate parent application 07/652,648, filed on 2/8/91.

Claims 28-29,31-32,38-40 and 42-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Ginsberg et al (5,177,188) in light of the AntiJen data base search.

Ginsberg et al show peptides of platelet glycoprotein GPIIIa which constitute B-cell epitopes recognized by autoantibodies in the sera of patients having Immune thrombocytopenic purpura. These autoantibodies are pathogenic in such patients (see col. 1, lines 15+). Claim 28 is thus anticipated.

The B-cell epitopes of SEQ ID NOS: 1 and 2 of Ginsberg et al inherently have no T-cell epitopes, as shown by a search of these sequences for T-cell epitopes in the AntiJen data base at **http://www.jenner.ac.uk/AntiJen/aj_tcell.htm**. Search results are pasted infra.

Nothing in applicant's contemplations of immunogen "analogs" rules out mere oligopeptides constituting B-cell epitopes. Claim 28 is thus anticipated.

Claims 38-39 are included because one of skill would reasonably expect that the recited T-cell stimulation index in each case would be inherently observed for a peptide lacking T-cell epitopes.

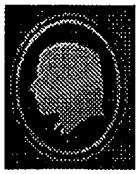
Regarding dependent claims 29 and 40, the Peptides of Ginsberg et al have side chain functional groups that would be suitable for coupling to a carrier. Also Ginsberg et al disclose derivatives with altered side chains that would likewise be suitable for coupling to a carrier (e.g. col.5, lines 16+) or with added amino acid residues suitable for coupling to a carrier (e.g. col. 8, lines 41+).

Regarding dependent claims 31 and 42, note col. 6, line 60-col. 7, line 7 and col. 18, lines 20-26.

Regarding dependent claims 32 and 43, complexes are formed in the disclosed assays (col. 9, line 58-col. 11, line 39).

For SEQ ID NO:1 of Ginsberg





**AntiJen** a kinetic, thermodynamic and cellular database

FULL SEARCH: T CELL EPITOPE

1 Enter an **epitope string** YHDRKEFAKFEE

- Replace variable amino acid positions with an asterisk (*).
- Encase alternative amino acids in square brackets e.g. [AEI]

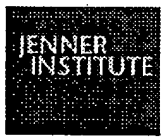
2 Enter the **length of amino acid string**
Leave blank to retrieve all. MIN MAX

3 Select the restriction **allele** or **serotype** CLASS-1

Search AntiJen

**New Search:** MHC Ligand MHC Kinetics T Cell Epitope TCR-MHC TAP Ligand Protein L
Discontinuous B Cell Epitope Diffusion Coefficient Peptide Libraries Copy Numb
AntiJen *BLAST Quick Search

[ Edward Jenner Institute ] [ Jenner Bioinformatics ] [ Links ] [ AntiJen Homepage ] [ Help ] [ C




Promoting Healt

For SEQ ID NO:1 of Ginsberg



THE EDWARD JENNER INSTITUTE for VACCINE RESEARCH

**AntiJen** a kinetic, thermodynamic and cellular database v2.0

THE ANTIJEN DATABASE SEARCH RESULTS

**You searched for epitope string "YHDRKEFAKFEEERARAKWDTANN" of undefined length.**

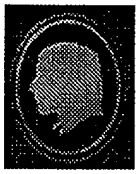
**Sorry there are no results for your search criteria**

Go to T Cell Epitope Full Search Page

Go to Quick Search & Home Page

For SEQ ID NO:1 of Ginsberg





# *AntiJen* a kinetic, thermodynamic and cellular database

FULL SEARCH: T CELL EPITOPE

1 Enter an **epitope string** YHDRKEFAKFEE

- Replace variable amino acid positions with an asterisk (*).
- Encase alternative amino acids in square brackets e.g. [AEI]

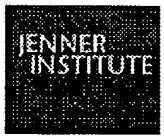
2 Enter the **length of amino acid string**
Leave blank to retrieve all. MIN [ ] MA

3 Select the restriction **allele** or **serotype** CLASS-2

Search AntiJen

**New Search:** MHC Ligand MHC Kinetics T Cell Epitope TCR-MHC TAP Ligand Protein L
Discontinuous B Cell Epitope Diffusion Coefficient Peptide Libraries Copy Numb
AntiJen *BLAST Quick Search

[ Edward Jenner Institute ] [ Jenner Bioinformatics ] [ Links ] [ AntiJen Homepage ] [ Help ] [ C




Promoting Healt

For SEQ ID NO:1 of Ginsberg



THE EDWARD JENNER INSTITUTE for VACCINE RESEARCH

***AntiJen*** a kinetic, thermodynamic and cellular database *v2.0*

**THE ANTIJEN DATABASE SEARCH RESULTS**

**You searched for epitope string "YHDRKEFAKFEEERARAKWDTANN" of undefined length.**

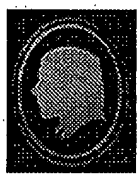
**Sorry there are no results for your search criteria**

Go to T Cell Epitope Full Search Page

Go to Quick Search & Home Page

For SEQ ID NO:2 of Ginsberg





# *AntiJen* a kinetic, thermodynamic and cellular database

FULL SEARCH: T CELL EPITOPE

1 Enter an **epitope string** ANNPLYKEATSTF

- Replace variable amino acid positions with an asterisk (*).
- Encase alternative amino acids in square brackets e.g. [AEI]

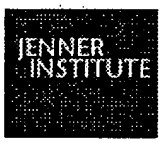
2 Enter the **length of amino acid string**
Leave blank to retrieve all. MIN MAX

3 Select the restriction **allele or serotype** CLASS-1

Search AntiJen

**New Search:** MHC Ligand MHC Kinetics T Cell Epitope TCR-MHC TAP Ligand Protein Ligand Discontinuous B Cell Epitope Diffusion Coefficient Peptide Libraries Copy Number AntiJen *BLAST Quick Search

[ Edward Jenner Institute ] [ Jenner Bioinformatics ] [ Links ] [ AntiJen Homepage ] [ Help ] [ C




Promoting Healt

For SEQ ID NO:2 of Ginsberg



THE EDWARD JENNER INSTITUTE for VACCINE RESEARCH

*AntiJen* a kinetic, thermodynamic and cellular database *v2.0*

THE ANTIJEN DATABASE SEARCH RESULTS

**You searched for epitope string "ANNPLYKEATSTFTNITYRGT" of undefined length.**

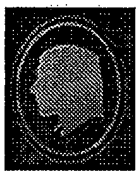
**Sorry there are no results for your search criteria**

Go to T Cell Epitope Full Search Page

Go to Quick Search & Home Page

For SEQ ID NO:2 of Ginsberg





# *AntiJen* a kinetic, thermodynamic and cellular database

FULL SEARCH: T CELL EPITOPE

1 Enter an epitope string ANNPLYKEATSTF

- Replace variable amino acid positions with an asterisk (*).
- Encase alternative amino acids in square brackets e.g. [AEI]

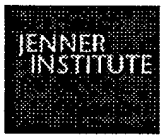
2 Enter the length of amino acid string
Leave blank to retrieve all. MIN MAX

3 Select the restriction allele or serotype CLASS-2

Search AntiJen

**New Search:** MHC Ligand MHC Kinetics T Cell Epitope TCR-MHC TAP Ligand Protein L
Discontinuous B Cell Epitope Diffusion Coefficient Peptide Libraries Copy Numb
AntiJen *BLAST Quick Search

[ Edward Jenner Institute ] [ Jenner Bioinformatics ] [ Links ] [ AntiJen Homepage ] [ Help ] [ C




Promoting Healt

For SEQ ID NO:2 of Ginsberg



THE EDWARD JENNER INSTITUTE for VACCINE RESEARCH

*AntiJen* a kinetic, thermodynamic and cellular database *v2.0*

**THE ANTIJEN DATABASE SEARCH RESULTS**

**You searched for epitope string "ANNPLYKEATSTFTNITYRGT" of undefined length.**

**Sorry there are no results for your search criteria**

Go to T Cell Epitope Full Search Page

Go to Quick Search & Home Page

Claims 28-29,31-32,38-40 and 42-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Dintzis et al (6,340,460 or 6022,544) in light of the AntiJen data base search.

For convenience, examiner will refer only to the '460 reference by col. And line numbers.

Dintzis et al show B-cell epitope containing peptides from Histone 2B, which is a target protein of an undesirable, autoimmune response; Dintzis et al indicate residues 3-12 as critical to the B-cell epitope. See Table 2, at cols 33-34; col. 33,lines 40-55; col. 49, lines 53-60; and col. 72, lines 1-50 (pages 51-53, 84 and 108-110 of earlier filed application 07/628,858 disclose likewise). This peptide segment inherently has no T-cell epitopes; see AntiJen search results for T-cell epitopes pasted infra.

Claims 38-39 are included because one of skill would reasonably expect that the recited T-cell stimulation index in each case would be inherently observed for a peptide lacking T-cell epitopes.

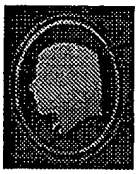
Regarding dependent claims 29 and 40, the Peptides of Dintzis et al have side chain functional groups that would be suitable for coupling to a carrier. Also Ginsberg et al disclose derivatives with added amino acid residues suitable for coupling to a carrier (e.g. col. 33, lines 40-55 and col. 38, line 43-col. 39, line 30).

Regarding dependent claims 31 and 42, note col. 39, lines 31-32.

Regarding dependent claims 32 and 43, complexes are formed in the disclosed assays (col. 32, lines 45-57).

SEQ ID NO:17 of Dintzis et al





# *AntiJen* a kinetic, thermodynamic and cellular database

FULL SEARCH: T CELL EPITOPE

1 Enter an **epitope string** EPAKSAPAPKKGI

- Replace variable amino acid positions with an asterisk (*).
- Encase alternative amino acids in square brackets e.g. [AEI]

2 Enter the **length of amino acid string**
Leave blank to retrieve all. MIN [ ] MA

3 Select the restriction **allele** or **serotype** H-2

Search AntiJen

**New Search:** MHC Ligand MHC Kinetics T Cell Epitope TCR-MHC TAP Ligand Protein L
Discontinuous B Cell Epitope Diffusion Coefficient Peptide Libraries Copy Numb
AntiJen *BLAST Quick Search

[ Edward Jenner Institute ] [ Jenner Bioinformatics ] [ Links ] [ AntiJen Homepage ] [ Help ] [ C

JENNER INSTITUTE

Promoting Healt

SEQ ID NO:17 of Dintzis et al



THE EDWARD JENNER INSTITUTE for VACCINE RESEARCH

*AntiJen* a kinetic, thermodynamic and cellular database *v2.0*

THE ANTIJEN DATABASE SEARCH RESULTS

**You searched for epitope string "EPAKSAPAPKKGEEC" of undefined length.**

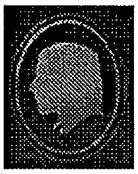
**Sorry there are no results for your search criteria**

Go to T Cell Epitope Full Search Page

Go to Quick Search & Home Page

SEQ ID NO:17 of Dintzis et al





# *AntiJen* a kinetic, thermodynamic and cellular database

FULL SEARCH: T CELL EPITOPE

1 Enter an **epitope string** EPAKSAPAPKKGI

- Replace variable amino acid positions with an asterisk (*).
- Encase alternative amino acids in square brackets e.g. [AEI]

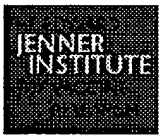
2 Enter the **length of amino acid string**
Leave blank to retrieve all. MIN MAX

3 Select the restriction **allele** or **serotype** I-A

Search AntiJen

**New Search:** MHC Ligand MHC Kinetics T Cell Epitope TCR-MHC TAP Ligand Protein Ir
Discontinuous B Cell Epitope Diffusion Coefficient Peptide Libraries Copy Numb
AntiJen *BLAST Quick Search

[ Edward Jenner Institute ] [ Jenner Bioinformatics ] [ Links ] [ AntiJen Homepage ] [ Help ] [ C




Promoting Healt

SEQ ID NO:17 of Dintzis et al



THE EDWARD JENNER INSTITUTE for VACCINE RESEARCH

***AntiJen*** a kinetic, thermodynamic and cellular database *v2.0*

**THE ANTIJEN DATABASE SEARCH RESULTS**

**You searched for epitope string "EPAKSAPAPKKGEEC" of undefined length.**

**Sorry there are no results for your search criteria**

Go to T Cell Epitope Full Search Page

Go to Quick Search & Home Page

Non-elected claims 33-37 have not been rejoined, since the claimed peptides can exist independently of the method of their making, irrespective of whether the limitations of the examined claims were to be entered into the non-elected claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, PhD whose telephone number is 571-272-0849. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on 571-272-0849. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Typed 9/22/05 DAS

David A Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT 182 1644